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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/067,482

02/07/2002

Zairen Sun

1U 102 R1

7159

23599

7590

10/21/2004

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EXAMINER

YAEN, CHRISTOPHER H

ART UNIT

PAPER NUMBER

1642

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

**Application No.**

10/067,482

**Applicant(s)**

SUN ET AL.

**Examiner**

Christopher H Yaen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 1-5 and 10-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 6-9 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

**Re: Sun et al**

**Priority Date: 7 February 2002**

1. The amendment filed 8/3/2004 is acknowledged and entered into the record. Accordingly, no claims have been canceled or added.
2. Claims 1-27 are pending, claims 1-5 and 10-27 are withdrawn as being drawn to a non-elected invention. Applicant is reminded to cancel claims drawn to non-elected inventions.
3. Claims 6-9 are examined on the merits.
4. The signed declaration under 35 CFR 1.132 filed 8/25/2004 is acknowledged.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

#### ***Claim Rejections Maintained***

#### ***35 USC § 101 & 35 USC § 112, 1<sup>st</sup> paragraph***

6. The rejection of claims 6-9 under 35 USC § 101 as lacking a substantial or well established utility is maintained for the reasons of record. Applicant argues that the instant invention has a clear and well established utility. Specifically, applicant argues that the utility encompasses use of the polypeptide as a marker for blood vessels and blood vessel formation. Applicant further argues that the polypeptides are useful for assessing vascularization in cancer biopsies. To substantiate the arguments, applicant relies on the *Revised Interim Utility Guidelines Training Materials*, wherein it is alleged that a marker that is specific for cancer substantiates the utility of the instant invention.

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Applicant's arguments have been carefully considered but are not deemed persuasive to overcome the rejection of record. The specification has only provided evidence of the up-regulation of the mRNA encoding the protein of the instant invention in tissues associated with angiogenesis. The specification has not provided one of skill in the art with any evidence that the up-regulation of the mRNA is in any way correlative to the up-regulation of the protein itself, nor provided any information on the protein, or whether the protein is translated at up-regulated levels. Thus the intended utility of the protein as a marker for angiogenesis or vasculogenesis has not been clearly set forth in the specification so that one of skill reading the disclosure of the instant invention is able to clearly determine that the utility is evident. Furthermore, because the protein has only been characterized to the extent that the protein has homology to other dehydrogenase proteins and would thus have similar activities to the dehydrogenase proteins, there is no evidence that the protein of the instant invention would have any activity similar to homologous proteins, and therefore no well established utility has been set forth for the protein of the instant invention.

Applicant's reliance on the *Revised Interim Utility Guidelines Training Materials* for support of their arguments is not persuasive in this case because example 12 (cited by the applicant), details instances where the protein has already been established as having an activity and has actually been shown to be differentially expressed in some tissue. In the instant case, the specification has only taught mRNA expression levels and has not provided any information of the protein's differential expression levels in angiogenic versus non-angiogenic tissue.

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In support for the applicant's statements of utility, attached hereto is a factual declaration under 37 CFR 1.132 by Dr. Zairen Sun (herein Sun Declaration) with examples of mRNA expression patterns derived from angiogenic tissue samples. The declaration demonstrates that the mRNA termed ANH401 is expressed at relatively low levels at times of non angiogenic activity and is highly expressed during times of angiogenesis. Based on this, the Sun Declaration concludes that the expression pattern is useful as a marker for angiogenesis as well as for determining the presence or absence of blood vessels in tumor biopsy samples. However, the declaration does not provide sufficient support for the utility of the protein itself. Absent any evidence of the protein's function, the protein's expression pattern, and any correlative data that would suggest that the mRNA is in any way related to the protein's expression level, the utility of the protein has not been provided and therefore a well established utility has not been set forth. If the claims had been drawn to the nucleic acids instead of the proteins, the disclosed utilities could have been attributed thereto. Thus the rejection of the claims under 35 USC 101 as lacking a credible or substantial utility is maintained.

Because the instant claims lack a well established or substantial utility, one of skill in the art would also not be able to make or use the invention. Therefore the rejection of the claims under 35 USC 112, 1<sup>st</sup> paragraph is also maintained.

### **NEW ARGUMENTS**

#### ***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

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7. Claims 8-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. THIS IS A NEW MATTER REJECTION. The claims of the instant invention have been amended to reflect an isolated human polypeptide comprising an amino acid that is 99% identical to the amino acid of SEQ ID No: 2 and which comprises the sequence of CDLFIQ (SEQ ID No: 2). The specification as filed does not specifically disclose any specific portion of SEQ ID No: 2, specifically the sequence of CDLFIQ, and thus such amendment to the claims does not find support in the specification as originally filed. Although the specification does disclose SEQ ID No: 2, no specific recitation of the sequence (i.e. CDLFIQ) newly added to the claims has been provided before the instant amendment. The specification only discloses the protein of SEQ ID No: 2 as a whole and the specific sequence (i.e. CDLFIQ) now claimed was not contemplated at the time of filing.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> paragraph***

8. Claims 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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9. Claim 8 and dependent claim 9 as newly amended recites "CDLFIQ (SEQ ID NO: 2)" as part of the invention. However, it is unclear as to whether SEQ ID No: 2 refers to the "CDLFIQ" sequence of the entire protein of which is 553 amino acids long.

Clarification and correction is required.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph***

10. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The written description in this case has only set forth an amino acid of SEQ ID No: 2 and therefore the claims are not commensurate in scope to the claims that read on an amino acid sequence that is 99% identical to that of SEQ ID No: 2.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural

features common to the members of the genus, which features constitute a substantial portion of the genus.”

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., \_\_\_ F.3d \_\_\_, 2004 WL 260813, at \*9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of protein sequences that encompass the genus of proteins that are 99% identical to SEQ ID No: 2 nor does it provide a description of structural features that are common to the proteins that are 99% identical to SEQ ID No: 2, nor does it teach a functional attribute that the proteins of which are 99% identical to SEQ ID No: 2 would include. Moreover, since the specification fails to provide information with regard to which amino acids are modified or are 1% different from that of SEQ ID No: 2, one of skill in the art cannot reasonably predict which sequences are modified and thus one of skill in the art cannot ascertain if the applicant was in possession of a representative number of species to represent a large genus of sequences. It is well known in the art that a single substitution in a protein. For example, a conservative replacement of a single “lysine” residue at position 118 of acidic fibroblast growth factor by “glutamic acid” led to the substantial loss of heparin binding, receptor binding and biological activity of the protein (Burgess et al., J of Cell Bio. 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply

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reduced the biological activity of the mitogen (Lazar et al. Molecular and Cellular Biology 8:1247-1252, 1988). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Because the specification has failed to provide one of skill in the art with any guidance in terms of which amino acids are critical to the functionality, or any core structure which is representative of the broad genus of proteins claimed, one of skill in the art would not be able to predictably determine if the applicant was in possession of what is now claimed.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the disclosure of one species (i.e. SEQ ID No: 2) is insufficient to describe the genus. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states “applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the ‘written description’ inquiry, *whatever is now claimed*.” (See page 1117.) The specification does not “clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of sequences that are at least 99% identical to SEQ ID No: 2, and

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therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a protein of SEQ ID NO:2, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

**All other rejections are withdrawn in view of the applicant's amendments and arguments thereto as set forth in a paper filed 8/3/2004.**

### **Conclusion**

No claim is allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher H Yaen whose telephone number is 571-272-0838. The examiner can normally be reached on Monday-Friday 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher Yaen  
Art Unit 1642  
October 12, 2004

A handwritten signature in black ink, appearing to read "Gary Nickol". The signature is stylized with a large initial "G" and a long, sweeping underline.

**GARY NICKOL**  
**PRIMARY EXAMINER**